Can adult intravenous feeds be safely administered over a continuous 48-hour period?

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Introduction

A number of influential recommendations not to administer lipid-containing intravenous feeds for any period exceeding 24 hours have been issued. Despite this, many centres continue to administer these feeds for longer than 24 hours which implies some controversy. The aim of this discussion is to explore the reasons behind the recommendations and to consider their relevance to clinical practice. It is important to note that throughout this discussion it is taken to be the case that giving sets are changed at the same time as the intravenous feed.

Background

The administration of intravenous feeds over a continuous 48-hour period could be expected to offer a number of benefits (**Figure 1**) even though various guidelines specifically advise against this practice. Whilst it is unlikely any centre would wish to prescribe every intravenous feed over 48 hours, there may be occasions when it could be beneficial to do so.

Tailored intravenous feeds are increasingly based on commercially available multichamber bags that can offer a number of advantages if used appropriately.[2] More recently, a greater variety of multichamber bags with lower energy contents are becoming available in some countries.

Nevertheless, in addition to a cost implication of using two bags when one would suffice (albeit with potentially extra pharmacy additions required), the current ranges may not provide what a patient clinically requires, for example, due to an inappropriate non-protein energy to protein expressed as nitrogen ratio.[2, 3]

A further example may be that of meeting the UK NICE Adult Nutrition Support Guidelines in some circumstances. These guidelines recommend starting patients at a maximum of 50% of estimated energy needs, and sometimes even lower, in order to reduce the risk of refeeding complications.[4] One potential option here is to administer a (part of a) relevant bag over a 48-hour period, whilst ensuring adequate electrolyte and micronutrient provision over each 24-hour period.

When discontinuing intravenous feeding due to patient progress, it is often continued but at a lower infusion rate before stopping completely. This is to limit the risk of rebound hypoglycaemia and to ensure progress does not slow or even stop. A possible solution to this would be to simply reduce the infusion rate of an existing bag resulting in administration beyond 24 hours.

Figure 1: Potential Benefits of Intravenous Feed Administration over 48 Hours

- Direct cost saving of feed bags as fewer used
- Fewer overall disposables required in pharmaceutical facilities to prepare fewer bags,[1] even with potentially greater volumes of additions
- Fewer aseptic manipulations on ward required to connect feed to patient (ward time saving)[1]
- Limiting the need for bespoke bags by more flexible use of locally kept stock bags to meet individual clinical patient needs

Note: Extra additions may be required to ensure adequate electrolyte / micronutrient provision over a 24-hour period

These examples illustrate occasions when part of a bag with a greater energy content over a duration beyond 24 hours might be indicated, providing that adequate electrolyte and micronutrient provision over a 24-hour period can be practically achieved. It is important to ensure that a system is in place for occasions when only a limited quantity of a bag is to be administered to avoid any risk of accidental administration of an excessive volume too quickly.

Current guidelines

The European Society for Parenteral and Enteral Nutrition (ESPEN) guidelines recommend changing giving sets every 24 hours for lipid-containing feeds, or every 72 hours for non-lipid containing feeds.[5] No specific comments regarding this are included but the authors note it as a Grade C recommendation, meaning it was made on the grounds of 'expert opinion and/or clinical experience of respected authorities'.

> It is known that parenteral doses prepared in clinical environments have a greater risk of microbial contamination than those prepared in dedicated pharmaceutical environments.[18]

The epic2 guidelines, commissioned by the UK Department of Health, also state that administration sets for lipid-containing intravenous feeds should be replaced at 24 hours, but that lipid-free regimens may be used for up to 72 hours.[6] However, unlike the ESPEN guidelines, the epic2 guidelines provide some further discussion around why they make this recommendation. They reason that lipid emulsions are an independent risk factor for microbial growth and subsequently catheter-related sepsis (CRS). One supporting reference is given: the 2002 'Guidelines for the Prevention of Intravascular Catheter-Related Infections' from the National Center for Infectious Diseases.[7] These American guidelines again recommend that giving sets for lipid-containing infusates are changed more frequently than 72-hourly, but offer no specific limit. Again they cite lipid as an independent risk factor for CRS and offer seven specific studies in support of this.[8-14]

The consensus of the above guidelines is that only giving sets for lipid-containing intravenous feeds need to be limited to 24-hour administration and the evidence for this is either expert opinion and/or that lipid is an independent risk factor for CRS because it readily supports microbial growth.

This could seem reasonable because a microbially contaminated intravenous dose can result in nosocomial bacteraemia, quickly make a patient very sick, or directly result in their death[15-17]

Interestingly, the guidelines themselves recommend intravenous feeds may be administered over up to 72 hours if they contain no lipid because the lipid might be a specific component increasing the risk of a contaminated feed. However, feeds without lipid will need to have a higher glucose content to make up the energy provision lost from the exclusion of a lipid component and this is clearly also a risk, yet the guidelines allow such feeds to run over up to 72 hours. Although extremely high glucose concentrations can have an antimicrobial effect it is very unlikely an intravenous feed would ever be of such a high concentration.

Whilst the recommendations all seem to be based around CRS risk, it is interesting to note that in no case does the actual probability of a contaminated intravenous feed appear to have been taken into account.

It is known that parenteral doses prepared in clinical environments have a greater risk of microbial contamination than those prepared in dedicated pharmaceutical environments.[18] Indeed, because of this idea, the UK National Patient Safety Agency (NPSA) guidelines[19] require any dose prepared for parenteral administration within a clinical environment to have a maximum 24-hour expiry. Additionally, the NPSA guidelines do not allow any intravenous feed preparation, or any additions to intravenous feeds, to be made in a clinical environment. Instead, feed preparation or aseptic additions to feeds must always be carried out within controlled and dedicated pharmaceutical units. These units must comply with appropriate and relevant standards such as those for unlicensed,[20] or those for licensed,[21] UK pharmaceutical units. The preparation or manipulation of intravenous feeds in this way results in an extremely low probability of microbial dose contamination, down to almost zero, with recommendations to aim to limit the chance to a maximum of one in 10,000 bags.[22]

Given the negligible risk of a microbially contaminated feed prepared in an appropriate environment, the major extrinsic risk factors for CRS become dose preparation in clinical environments (as above), and inappropriate handling of the *in situ* intravenous catheter.

Whilst some try to justify preparing, or making additions to, intravenous feeds in a clinical environment[23] this author believes this can never be justified.[24] This means that this practice is not a significant risk simply because it does not happen. If it does happen the patient would be put at very considerable risk and should, therefore, be transferred to a centre where intravenous feeding can be carried out more safely.

Given that there is a negligible risk of a patient receiving a feed that has been contaminated during preparation in an appropriate environment, the guidelines, therefore, imply this remains a greater risk than that of intravenous catheter manipulation twice rather than once (the extra manipulation resulting from two bags over 48 hours rather than just one). Is this the case in practice? The answer to this question would not appear to be as straightforward as the guidelines suggest.

It is clear that should the intravenous feed become microbially contaminated, either during preparation or manipulation in a clinical environment (such as the addition of a giving set or connecting the bag to the intravenous catheter), there is likely to be a greater risk resulting from feed administration over 48 hours rather than 24 hours. This is because of the potential additional time available for multiplication of the bacteria or fungi before possible infusion into the patient, although it is plausible with appropriate patient monitoring for CRS this would be detected either way.

This complicates the picture because if poor aseptic techniques are used to administer intravenous feeds to patients the risk could be much greater.

Inappropriate handling of intravenous catheters in hospitals is likely to be one of the most significant factors contributing to high CRS rates. However, it should be noted that intravenous feeds are often treated differently to other infusates. Indeed, particular care should be taken when aseptically manipulating intravenous feeds and intravenous access used for intravenous feeds. Lack of staff (time), training, skill or understanding can often be the reality so it is important to have strict policies and protocols in place to limit any risk these factors may present to the intravenous feed. For example, limiting these risk factors always requires a full aseptic non-touch technique when adding giving sets or connecting the feed to the patient's intravenous catheter rather than considering the use of a simple 'non-touch'

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Figure 2: The Catheter-related Sepsis Risk Question with Running Intravenous Feeds over 48 Hours

Does the greater risk of catheter-related sepsis lie with microbial feed contamination during preparation or with increasing the number of times the intravenous access is manipulated?

Figure 3: Appropriate Clinical Care of Patients being Fed Intravenously before Considering Administration of Intravenous Feeds over 48 Hours

- Appropriate pharmaceutical facilities to prepare, or make additions to, all intravenous feeds[19]
- Absolutely no preparation of, or additions to, intravenous feeds within a clinical environment[19]
- Appropriate policy to monitor for, and action to be taken in the event of, either suspected or actual catheter-related sepsis[25]
- Appropriate aseptic manipulation within clinical environments using a full aseptic non-touch technique rather than a simple non-touch technique supported by relevant policies and protocols
- A new giving set with each new intravenous feed bag used (preferably inserted into the bag in dedicated pharmaceutical facilities to further limit sepsis risk)
- Ensuring adequate total electrolyte and micronutrient bag content to allow appropriate provision over a 24 hour period for each individual patient
- Appropriate stability available for the intravenous feed over a 48 hour period at room temperature
- Ensuring minimal air in intravenous feed bag during preparation, and insertion of giving set, to limit chemical instability (particularly ascorbic acid degradation)[26]
- Confirmation from the giving set manufacturer of 48-hour compatibility with intravenous feeds
- Systems in place to prevent any bag being administered beyond 48 hours
- Systems in place to prevent inadvertent excessive feed administration

technique. Nevertheless, despite such policies and protocols, the risk is never absolutely zero; and it is likely to be this risk that requires comparison to the risk of microbial feed contamination during preparation when determining whether administration of intravenous feeds over 48 hours is reasonable from a CRS risk point of view (**Figure 2**). Should aseptic manipulations connecting the intravenous feed to the patient result in a CRS episode, with appropriate clinical monitoring it is likely to be noted sooner rather than later should it be clinically significant, whether the feed is administered over either 24 or 48 hours.

Other factors

This discussion has focused on CRS risk but there are also other factors that may influence whether it is reasonable to administer intravenous feeds over a 48-hour period.

Some compatibility issues between the intravenous feed and certain giving sets may be of relevance although modern sets are generally compatible over a 48-hour period. Advice can be obtained from the manufacturer of the giving sets used locally.

Logistics must always be taken into account to ensure the 'cold chain' is maintained at all times and particular attention needs to be given to this aspect when running intravenous feeds over 48 hours as the feed may 'only just' be stable for 48 hours at room temperature. This would mean that there is a room temperature stability 'time safety buffer' for 24-hour administration but this may be much more limited, or even lost, when running bags over 48 hours. Actual stability data should be readily available from the relevant feed manufacturer.

Some intravenous feed manufacturers may recommend against administration of intravenous feeds over 48 hours and, where this is the case, it is important to ask the reason. Clearly, if it is because of an issue such as physical incompatibility between the feed and the bag, or giving set plastics, or alternatively incompatibility developing within the feed itself, it would not be reasonable to go against this advice. However, it may be because any one of several guidelines recommend against the administration of a lipid-containing bag over longer than 24 hours. In this case, the questions then become whether the relevant guideline is mandatory for local services, and if not, whether it is both safe and clinically indicated to carry out a practice that would be inconsistent with the relevant guideline.

Conclusion

With appropriate clinical care and certain assurances from the intravenous feed and giving set manufacturer (Figure 3), it would appear logical that current guidelines limiting lipid-containing intravenous feeds to 24-hour infusion be reviewed to:

Firstly, specifically consider whether the CRS risk is judged to be greater by increasing the number of aseptic manipulations of the intravenous line, or whether the risk of a contaminated intravenous feed is greater.

Secondly, specifically consider other factors that may influence administration of intravenous feeds over 48 hours and make appropriate recommendations for their management.

Please note the views expressed are those of the author not of the BPNG.

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